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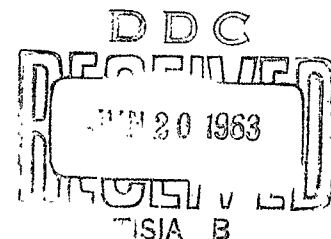
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ACTIVATION AND SUPPRESSION OF
SHIVERING DURING SEPTAL AND
HYPOTHALAMIC STIMULATION

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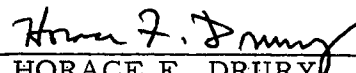
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ABSTRACT

In acute experiments on 38 lightly anesthetized cats, the
septal region of the forebrain and the hypothalamus were
explored for loci whose activation by electrical stimulation
produced, suppressed or failed to affect shivering. Shiver-
ing was consistently and repeatedly produced by stimulation
of the dorso-medial region of the posterior hypothalamus,
and sometimes by stimulation of the ventrolateral region of
the septum. A greater intensity of stimulus was needed to
produce more latent and less intense shivering during septal
than during hypothalamic stimulation. Similarly, more
intense stimulation was necessary to suppress shivering
during ventromedial septal stimulation than during anterior,
or ventrolateral posterior hypothalamic stimulation. The
most effective stimulation frequency for both activation and
suppression of shivering was 50 pulses/sec, i.e. fivefold
the evoked or suppressed limb tremor frequency. On the
basis of these results it was concluded that septal influences
on shivering are secondary to a primary hypothalamic modu-
lation of this tremor. Such modulation appears to be more
concerned with initiation and maintenance than with the rhythm
of shivering.

PUBLICATION REVIEW

HORACE F. DRURY
Director of Research

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ACTIVATION AND SUPPRESSION OF SHIVERING DURING SEPTAL AND HYPOTHALAMIC STIMULATION *

SECTION 1. INTRODUCTION

Shivering, induced in homeotherms by cooling, is an involuntary tremor whose function is the production of body heat. Here are reported experiments designed to localize the specific region of the brain primarily involved in its efferent (motor) control. Lesion experiments have demonstrated that decorticate (Aring, 1935; Bard, 1933; Pinkston et al, 1934; Stuart, 1961), thalectomized (Clark et al, 1939), and animals with anterior hypothalamic lesions (Bazett et al, 1933; Clark et al, 1939; Keller and Hare, 1932) can shiver, but that decerebrate preparations cannot (Bard, 1961; Stuart, 1961). The results of those investigators studying the effects of posterior hypothalamic lesions on shivering conflict on localizing the essential neurons to the dorsal posterior hypothalamus (Bazett et al, 1933; Keller and Hare, 1932), the ventromedial mid-hypothalamus (Frazier et al, 1936), the lateral posterior hypothalamus (Clark et al, 1939), and the ventrolateral posterior hypothalamus (Birzis and Hemingway, 1956).

Some investigators have studied this problem by stimulating the intact brain to instigate shivering. In three laboratories (Chatonnet, 1961; Hammel et al, 1960; Kundt et al, 1957), shivering has been evoked by thermal stimulation, but this technique does not permit a precise localization of the effective region. Others have demonstrated the production of shivering during electrical stimulation of the forebrain septum in anesthetized cats (Akert and Kesselring, 1951) and unanesthetized goats (Andersson, 1957), and the midbrain and pons in anesthetized cats (Birzis and Hemingway, 1957a). In the studies using cats, production of shivering by stimulation of the hypothalamus was mentioned. In each case only one hypothalamic locus was stimulated. These studies were devoted mainly to regions more rostral or more caudal than the hypothalamus. Since decorticate preparations with the septum destroyed can shiver (Bard, 1961; Dusser de Barenne, 1920; Stuart, 1961), it would seem that the most rostral region whose stimulation has been shown to consistently produce shivering is the septum. However, its ablation does not affect shivering. Anatomically this region of the forebrain, which is but a vestige in man (septum pellucidum), has been shown to have intimate connections with neocortical and rhinencephalic pathways to and from the thalamus, hypothalamus and midbrain (Fox, 1943;

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* Submitted for publication August 1961.

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Pribram and Kruger, 1954). Thus, it might well be, but is not proved, that the septum is involved in alterations in temperature regulation evoked by classical Pavlovian conditioning (Bykov, 1957), the production of shivering by hypnotic suggestion (Gessler and Hansen, 1927), and "psychological aspects" to cold tolerance mentioned in recent reports of human adaptation to cold stress (Scholander et al, 1958; Wyndham and Morrison, 1958).

However, if the septum is involved in the production of shivering, its activity should be secondary to hypothalamic activity in that it can be ablated without affecting shivering, and all known caudally projecting septal efferents synapse in the hypothalamus and thalamus (Nauta, 1958). Although there are some fornical fibers that project through both the septum and hypothalamus to make direct connections with the midbrain (Nauta, 1958; Sprague and Meyer, 1950), neither these fibers nor those septal projections to the thalamus could produce shivering, since the thalamus and also the hippocampus, from which the fornical fibers arise, can be ablated without affecting the production of shivering. Anterior hypothalamic stimulation, either thermal (Hemingway et al, 1940; Magoun et al, 1938) or electrical (Andersson et al, 1956; Hemingway et al, 1954), is known to suppress shivering. There are septal projections to both anterior and posterior hypothalamic regions. Therefore, if septal stimulation can evoke shivering, it should also be capable of suppressing it. Such suppression has been observed during septal stimulation (Hemingway et al, 1954) and during stimulation of more rostral telencephalic structures, the orbito-frontal gyrus (Kaada, 1951) and the amygdala (McLean et al, 1953). It is not known if the neurons activated to suppress shivering during stimulation of these two latter structures traverse the septum or relay within it.

On the basis of these anatomical and physiological studies, it appeared that septal production and suppression of shivering should be secondary to hypothalamic production and suppression. Secondly, if septal and midbrain electrical stimulation could produce shivering, so should stimulation of the hypothalamus. It was felt that the use of electrical stimulation would permit a localization of that region of the hypothalamus primarily responsible for the production of shivering.

This is a report of the results of experiments on 38 anesthetized cats in whom shivering was produced, or spontaneous shivering suppressed, during electrical stimulation of septal and hypothalamic loci. There were three stages to this investigation: (1) Localization of the hypothalamic region that produced shivering, when activated by electrical stimulation; (2) comparison of somatomotor effects produced during stimulation of the septum and the hypothalamus; and (3) comparison of the stimulus intensity required to suppress spontaneous shivering during septal and hypothalamic stimulation.

SECTION 2. METHODS

An attempt was made to produce shivering by electrical stimulation of hypothalamic sites in 20 anesthetized cats. The brain of each preparation was stimulated with a stainless steel concentric bipolar electrode insulated but for 0.5 mm of each tip. The outer cylinder of each electrode had a diameter of 0.4 mm and a thickness of 0.14 mm. The insulated inner wire was 0.1 mm in diameter. The distance between the tips was 0.5 to 0.75 mm. The resistance of each electrode was 30-50 K ohms in 0.9 per cent saline. The electrode could be connected either to a pen-writing electroencephalograph (Grass Instrument Co., Model III D) or to a stimulator and current monitor oscilloscope (Heath Co., Model OL-1). The stimulator (Grass Instrument Co., Model S 4C) produced square wave stimulating currents whose frequency, duration and intensity could be regulated. To detect shivering and other motor responses, electromyograms of fore and hind limbs were recorded. Respiration rate was recorded by a strain guage transducer (Statham Laboratory, Model P 23 B) connected to a rubber chest tambour. Fronto-occipital waves were recorded from stainless steel electrodes that pierced the calverium above the medial edge of the sigmoid gyrus and the posterior margin of the suprasylvian gyrus. The preparations were anesthetized with either alpha chloralose (40-60 mg/kg I. P.) or pentobarbital sodium (35 mg/kg I. P.). The head was then mounted in a stereotaxic frame, the scalp incised, the temporal muscles retracted and sufficient bone removed to expose the dorsal extent of the marginal gyrus. The dura was minutely cut to permit passage of the electrode into neural tissue. The electrode was stereotactically lowered into the hypothalamus which was stimulated at sites 0.5, 1.5, and 3.5 mm from the midline. Each stimulated locus was at least 1 mm distant from other stimulated loci. Rectal temperature was maintained at 37.5° to 38.5° C by appropriate adjustments of environmental temperature.

In five experiments the septal region was explored for loci which, when stimulated, produced either an increase in muscle tone or shivering. Responses evoked by stimulation of septal loci were compared to the response obtained during stimulation of the posterior hypothalamus. Comparisons included the latency and intensity of the response and the stimulus intensity necessary to evoke it. In some experiments a comparison was made of alterations in heart and respiration rates produced by such stimulation. In two of these experiments limited posterior hypothalamic mapping was also undertaken. In two further experiments comparisons were not made after extensive septal mapping, but rather the electrodes were oriented to septal loci where stimulation had produced motor changes in previous experiments.

In eight experiments on anesthetized animals that were shivering spontaneously in the cold, the septum was explored for sites whose stimulation suppressed or facilitated shivering. Shivering occurred in the waning stages of anesthesia when the rectal temperature of each animal was maintained at 33° to 36° C by alteration of environmental temperature. During these experiments a stimulus was not applied until shivering had been continuous in at least one limb for a period of five minutes. In six additional experiments the intensities of stimulation necessary to suppress shivering during septal, anterior and posterior hypothalamic stimulation were compared. In two experiments the relative inhibitory effects of varying stimulating frequency and pulse duration were noted.

At the termination of each experiment the brain was fixed in formalin, sectioned every 80 μ in the plane of the electrode tracts, and alternate sections stained with buffered thionine. Table I is a key to abbreviations of nomenclature used in schemata of stimulated sites.

SECTION 3. RESULTS

Localization of Hypothalamic Region Involved in Production of Shivering

Figure 1 shows the production of shivering when a posterior hypothalamic locus was stimulated and additionally illustrates the necessity for a long delay (12 hours) between induction of alpha chloralose anesthesia and initial stimulation. Shivering was bilateral when induced by ipsilateral brain stimulation. It was sometimes evident in the forelimbs before the hindlimbs and vice versa, but repeated stimulation of a hypothalamic locus always evoked the same patterns of fore- and hindlimb effects. Figure 2 lists the motor responses evoked by stimulation of posterior hypothalamic loci in six cats. Similar responses were obtained in 13 other cats. Each locus shown is 2 mm ventral to any other locus in the same vertical plane. In all cases stimulation along a tract was carried out at 1 mm depth intervals. Responses to stimulation of these intermediate loci are not shown because of the limitations involved in comparing specific loci stimulated in different experiments (Stuart, 1961). In this Figure, motor responses reported are a generalized increase in muscle tone, arrythmic muscle twitching, alternating tremor and shivering. Alternating tremor is defined as 4-7 cps limb tremor in which antagonistic muscles contract alternately. In shivering the tremor rate is faster (9-11 cps) and antagonistic muscles contract synchronously (Stuart et al, 1961a). Differences between these tremors were obvious both visually and electromyographically. Alpha chloralose customarily evoked muscle twitching as animals entered and emerged from an anesthetic state. No stimuli were applied at

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TABLE I. NOMENCLATURE: KEY TO ABBREVIATIONS

AC	commissura anterior	OC	chiasma opticum
Acb	N. accumbens	OT	tractus opticus
CC	corpus callosum	PC	commissura posterior
Cd	N. caudatus	Ped	Pedunculus cerebralis
CI	capsula interna	PO	regio praeoptica
CM	N. centrum medianum	Pul	Pulvinar
DBB	Diagonal band of Broca	Put	Putanem
En	N. entopeduncularis	R	N. Reticularis
Fcd	Fundis caudati	Re	N. reuniens
Fx	fornix	S	Stria medullaris
GL	geniculatum laterale	Spt	area septalis
GP	Globus pallidus	Sn	Substantia nigra
LME	Lamina medullaris externa	Su	N. subthalamicus
MI	massa intermedia	TMT	tractus mamillo-thalamicus
Mm	corpus mamillare	Vm	N. ventralis postero-lateralis
NCM	N. centralis medialis	VPM	N. ventralis postero-medialis
NPr	N. prothalamicus	Zi	Zona incerta
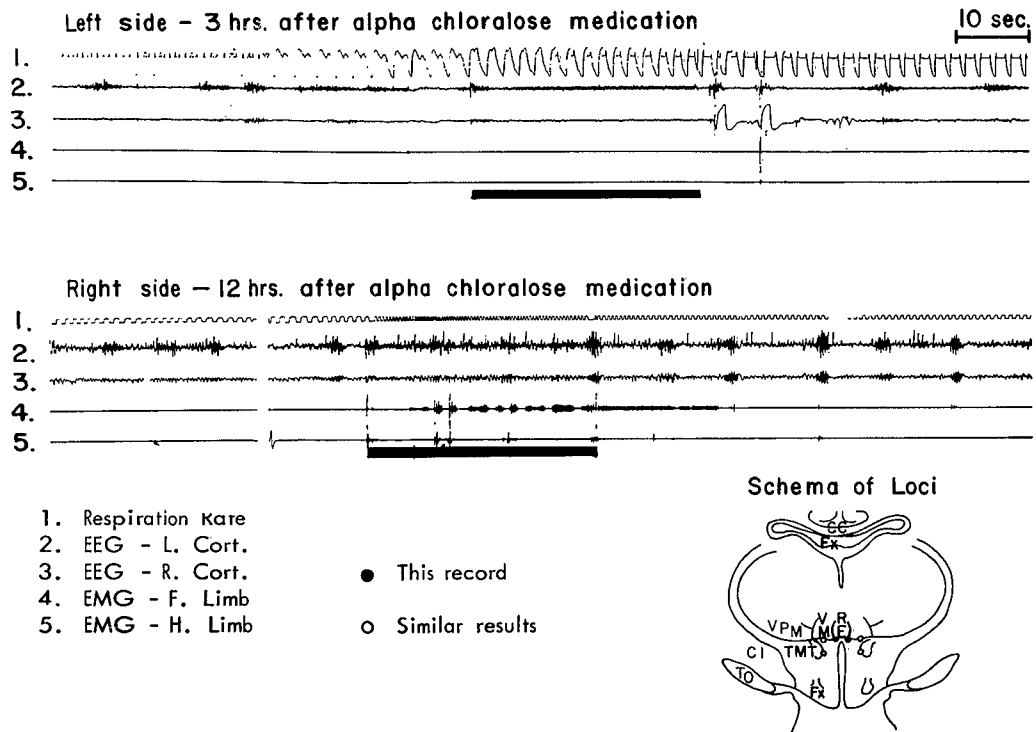
FIGURE 1. Responses to posterior hypothalamic stimulation 3 and 12 hours after induction of alpha chloralose anesthesia (50 mg/kg I. P.). Thick line indicates duration of stimulus (800 μ Amp/pulse-3 msec. pulses - 50 pulses/sec.). Three hours after drug administration stimulus evoked an increase in respiration rate and depth and a desynchronization of right and left side fronto-occipital EEG waves. Nine hours later, when a stimulus of the same parameters was applied to a contralateral site, shivering was evoked, in addition to the above.

CAT NO.	LOCUS																	
	1	2	3	4	5	6	7	8*	9	10	11	12	13	14†	15	16	17	18
ST. 7				TW	TW		O	SH	O									
ST. 9	O	TR	TO	TR	TO	O	O	SH	TW	TO	TR	TO	SH	TO	O	TO	TO	O
ST. 10	TO	TW		SH	SH		O	SH	O	TR	TR	TO	SH	SH	O	TO	SH	TO
ST. 11	TO	TO		TW	TW	O	O	SH	O	TO	TO	TO	SH	SH	O	O	SH	O
ST. 13										TO	TO		O	SH		O	SH	
ST. 17														TO	SH		O	SH	O

TO – Increase in muscle tone
TW – Muscle twitching
TR – Alternating tremor
SH – Shivering
O – No motor response
* – Stimulation produced shivering
    in cats No. ST. 5, 15 and 20.
† – Stimulation produced shivering
    in cats No. ST. 14, 18, 21,
    23, 24, 31ᵃ, 32ᵃ, 33ᵃ, 33ᵇ.
    and 38.

Schema of Loci

Plane A   Plane B
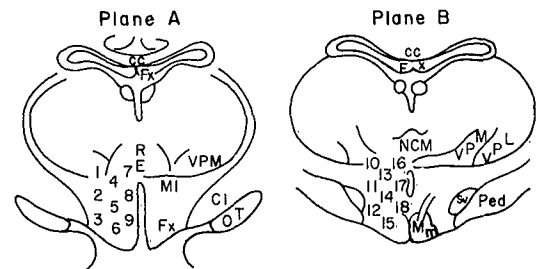
FIGURE 2. Responses to stimulation of posterior hypothalamic loci. Planes A and B are 10 and 9 mm anterior to the interauricular line respectively. Loci 1, 2 and 3 and 10, 11 and 12 are 2.5 mm from the midline. Loci 4, 5 and 6 and 13, 14 and 15 are 1.5 mm from the midline, while loci 7, 8 and 9 and 16, 17 and 18 are 0.5 mm from the midline. Loci 1 and 7 and 10 and 16 are 10 mm dorsal to the interauricular line, and loci 4 and 13 are 9 mm dorsal to this line.

these times. In any one preparation repeated stimulation of the same locus produced the same response. Shivering was most consistently produced by stimulation of loci within a diencephalic region 9 to 10 mm anterior and 7 to 9 mm dorsal to the interauricular line and 0 to 1.5 mm lateral to the midline. This region is bordered by ventral thalamic, dorsal hypothalamic and medial subthalamic structures. Systematic exploration of a plane 11 mm anterior to the interauricular line was attempted in five cats but shivering could not be evoked. In two cats stimulation of sites 1 mm caudal to loci 14 and 17 evoked shivering. Loci 3.5 mm lateral to the midline in frontal planes corresponding to A and B were stimulated in two cats without evoking shivering.

Stimulation of this region of the posterior hypothalamus produced shivering in cats anesthetized with pentobarbital sodium, but it was difficult to conduct mapping experiments in animals so anesthetized. Shivering could not be induced during deep pentobarbital anesthesia (1 to 2 hours after induction). When animals were "light" enough to shiver during hypo-thalamic stimulation (3 to 4 hours after induction of anesthesia), they were also capable of shivering spontaneously even when the rectal temperature was maintained at 37.5° to 38.5° C. Thus, it was impossible to maintain a nonshivering control state prior to the application of a stimulus and the augmentation of shivering during stimulation of any locus was of question-able significance. For this reason mapping experiments for stimulation of shivering were not attempted in preparations under pentobarbital sodium anesthesia.

The parameters of stimulation were constant in each experiment but the intensity of stimulation necessary to evoke shivering varied from animal to animal, ranging from 200 to 1600 μAmp/pulse, depending on the level of anesthesia. The frequency of stimulation utilized ranged from 25 to 100 pulses/sec. In some experiments 25 p/sec seemed more effective in evoking shivering than 50 or 100 p/sec. In other experiments 50 p/sec seemed the most effective. In two experiments this was examined more critically. Figure 3 illustrates an experiment in which the minimum stimulus inten-sities necessary to evoke shivering at various frequencies were determined. Stimuli of 50 and 100 p/sec required less intensity to evoke shivering than stimuli of 10, 25 and 200 p/sec. The best shivering response evoked by 10 p/sec stimulation lacked continuity. Conversely the maximal response evoked by 200 p/sec stimulation was a tremor in which background muscle tone predominated over phasic shivering activity. In another similar experiment shivering could not be evoked with 10 p/sec stimuli of 1600 μAmp/pulse intensity. It could be evoked with 25 and 50 p/sec stimuli of 400 μAmp/pulse intensity. In this experiment less intense stimuli were necessary at 25 and 50 p/sec than at 100 p/sec.
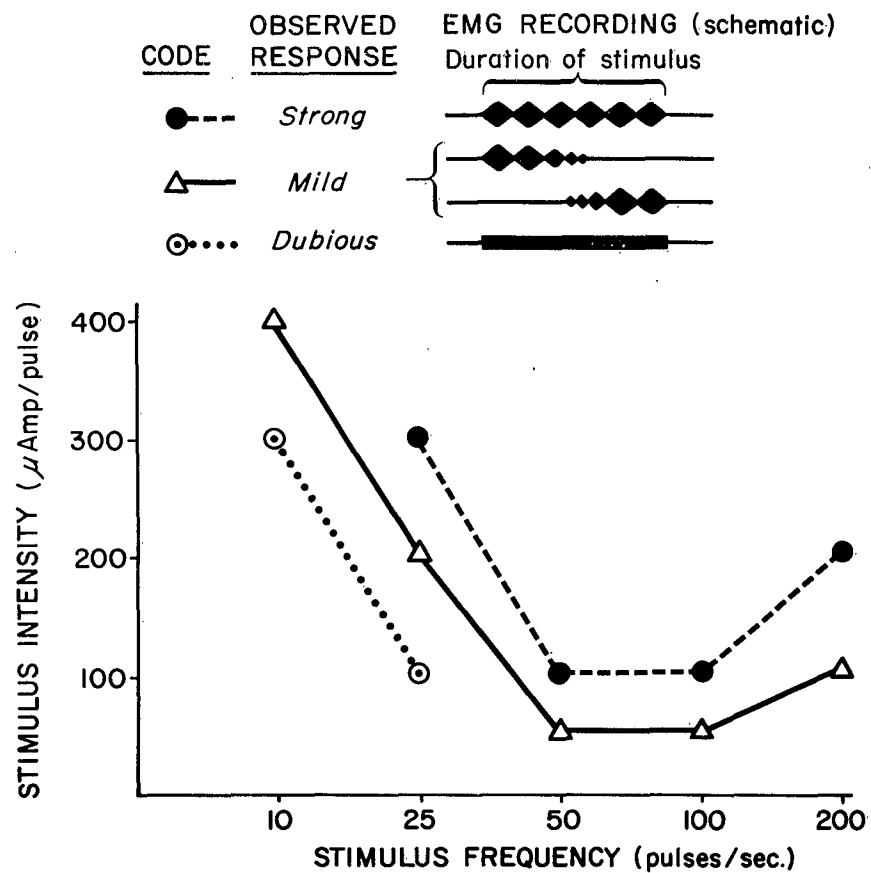
FIGURE 3. Effects of various stimulus frequencies and intensities on the shivering response to stimulation of a single posterior hypothalamic locus. If the EMG of at least one limb muscle showed a visible shivering pattern throughout the period of stimulation (30 sec. -1 msec. pulses), the response was considered "strong" and coded as a filled-in circle. If visible shivering had a latency of onset or ended before the stimulus was terminated, the response was considered "mild" and coded with an open circle. If the muscle response could not be classified as shivering or an increase in muscle tone, it was considered "dubious" and coded with a small filled-in circle.

Comparison of Somatomotor Responses to Septal and Posterior Hypothalamic Stimulation

Figure 4 lists the responses evoked by septal stimulation in five cats. As with the posterior hypothalamus, loci were stimulated at 1 mm depth intervals. Responses to stimulation of loci closer than 2 mms are not listed for the previously mentioned reason. Extensive mapping was also undertaken at a fontral plane intermediate to those shown in the Figure (i. e. a plane 15 mm anterior to the interauricular line). The responses to stimulation of loci in this plane are not listed because they were similar to those seen while stimulating plane A. Shivering was observed during stimulation of three of these cats. The response was best evoked by stimulation of a septal region 16 to 15 mm anterior and 13 to 9 mm dorsal to the interauricular line and 1.5 mm lateral to the midline. Shivering was also evoked by stimulation of loci 1 mm caudal to this region while stimulation of loci 1 mm more rostral evoked an increase in muscle tone but not shivering. It was of equal intensity and duration on both sides of the body during ipsilateral stimulation. Table II lists comparisons of effects produced during stimulation of the most "active" septal locus and a dorsomedial posterior hypothalamic locus. In four cats in which shivering was not produced by septal stimulation, it was observed during hypothalamic stimulation. In three cats in which shivering appeared during septal stimulation, it appeared with greater vigor and less latency of onset in response to the same or less intense stimulation of the posterior hypothalamus (Figure 5). In cat ST. 5 (Table II), the comparison is hardly valid in that the septum was stimulated 3. 5 hours after the induction of alpha chloralose anesthesia and the hypothalamus was stimulated 6 hours later. The cat may have been at too deep a level of anesthesia to shiver during septal stimulation. In the other experiments the stimuli were applied to septal and hypothalamic loci within a very short time of each other. Respiration and heart rate increases were of greater magnitude during posterior hypothalamic stimulation than during septal stimulation (Table II).

Suppression of Shivering during Septal and Hypothalamic Stimulation

In exploration of the septum and hypothalamus for loci whose activation suppressed shivering, the cats were anesthetized with pentobarbital sodium because spontaneous shivering occurs readily in the waning stages of such anesthesia. If the intensity of stimulation necessary to suppress shivering was to be kept constant in each mapping experiment, it was important that such an experiment be conducted in as short a time as possible so that the preparation could be stimulated at a relatively constant level of anesthesia. It was arbitrarily decided that no locus would be stimulated until shivering had been active and continuous for the preceding five minutes. Therefore, it was necessary to utilize a stimulus intensity that would clearly produce a

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CAT NO.	LOCUS															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
ST. 5	TO	TO	TO	TO	O	O	O	O								
ST. 13									TO	O	O	TO	TO	O	O	O
ST. 14	TO	SH	TO	SH	O	TO	O	O	TO	TO	TO	TO	O	O	O	O
ST. 15	O	O	O	SH	O	O	O	O	O	O	O	O	O	O	O	O
ST. 17	TO	SH	SH	SH	O	O	O	O	O	O	O	SH	O	O	O	O

TO – Increase in muscle tone
SH – Shivering
O – No somatic response
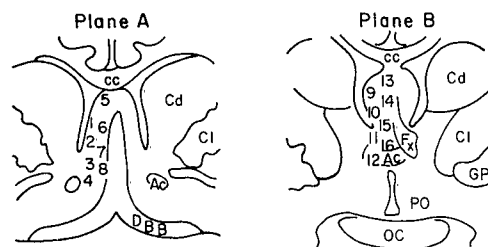
Schema of Loci

Plane A   Plane B

FIGURE 4. Responses to stimulation of septal loci. Planes A and B are 16 and 14 mm anterior to the interauricular line respectively. Loci 1, 2, 3 and 4 and 9, 10, 11 and 12 are 1.5 mm from the midline, while loci 5, 6, 7 and 8 and 13, 14, 15 and 16 are 0. 5 mm from the midline. Loci 1 and 9 are 15 mm dorsal, and loci 5 and 13, dorsal to this line. Loci ventral to the above are at 2 mm depth intervals.
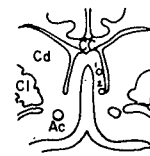
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TABLE II   COMPARISON OF EFFECTS OF SEPTAL AND POSTERIOR HYPOTHALAMIC
STIMULATION ON SOMATOMOTOR ACTIVITY, HEART AND RESPIRATION RATE

Cat No.	I.P. Dose of Alpha Chloralose in mg./kg.	Site Stimulated	Time in Hours after Induction of Anesthesia	Rectal Temp. in °C	Environ. Temp. in °C	Intensity in µA/Pulse	Pulse duration in msec.	Pulse freq. in pulses/sec.	Stimulus duration in sec.	Resp. Before stimulus	Resp. During stimulus	Resp. Δ	Heart Before stimulus	Heart During stimulus	Heart Δ	Observations of Somatomotor Activity
ST.5	65	Septum	3.5	37.9	27.8	1600	3	100	30	24	26	+2	210	210	0	Increase in muscle tone
		P. Hypothalamus	9.0	38.6	29.0	1600	3	100	90	28	34	+6	216	246	+30	Shivering after 25 sec. lat.
ST.13	95	Septum	24.0	36.8	29.5	1600	3	100	30	16	18	+2	- No data -			Incr. in hind limb twitching
		P. Hypothalamus	25.0	37.0	29.5	800	3	100	30	14q	17	+3				Increase in muscle tone
			25.1	37.0	29.5	1600	3	100	30	14	48	+30				Continuous shivering
ST.14	50	Septum	16.3	38.6	28.8	1600	3	100	36	12	22	+10	- No data -			Mild shivering
		P. Hypothalamus	17.1	38.4	28.2	800	3	100	23	24	50	+26				Shivering
ST.15	63	Septum	20.0	37.6	29.2	1600	3	100	35	36	40	+14	168	168	0	Mild shivering
		P. Hypothalamus	20.3	37.6	29.2	1600	3	100	30	33	60	+30	172	216	+44	Continuous shivering
ST.17	60	Septum 1	23.5	37.8	28.0	1600	3	100	30	12	12	0	114	102	-12	Mild shiv. 45 secs. after stim.
		Septum 2	23.6	37.8	28.0	1600	3	100	60	12	14	+2	1142	120	+6	Mild shivering
		P. Hypothal. 2	22.3	37.8	28.0	800	3	50	60	16	40	+30	96	156	+60	Continuous shivering
		P. Hypothal. 1	24.5	38.8	28.0	800	3	50	60	14	28	+14	164	192	+28	Continuous shivering
ST.18	50	Septum	24.5	36.2	28.0	1600	3	50	30	18	18	0	- No data -	174	0	Two muscle twitches
		P. Hypothalamus	25.0	36.0	28.0	800	3	50	30	20	36	+18	174			Mild shiv. post stimulation
ST.24	35 mg./kg. (pentobarbital sodium)	Septum	6.0	32.5	28.0	1600	1	50	60	26	18	-6	- No data -	156		No response
		P. Hypothalamus	6.0	32.5	38.0	1600	1	50	60	26	18	-6	154	156	+2	Shivering - continuous

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1. Respiration Rate
2. EEG – L. Cortex
3. EEG – R. Cortex
4. EMG – L. Forelimb
5. EMG – L. Hindlimb

Black line – Stimulus Duration
All stimuli 50 pulses/sec.
Pulse duration 3 msec.

Septum

P. Hypothalamus

Posterior Hypothalamus 2-800 μA/pulse
1.
2.
3.

100 μV   10 sec.

Septum 1- 1600 μA/pulse
1.
2.

4.
5.

Posterior Hypothalamus 1- 800 μA/pulse
1.
2.
3.
4.
5.

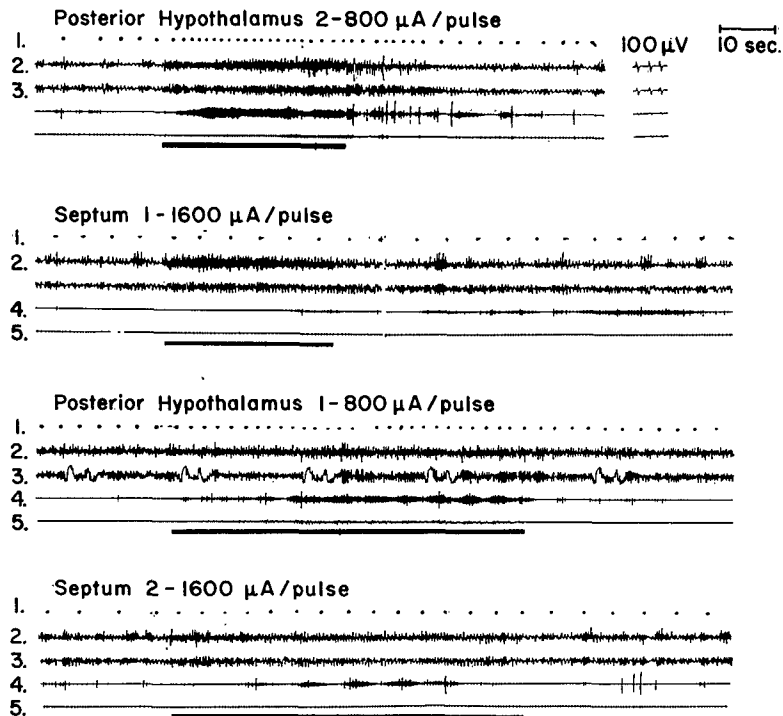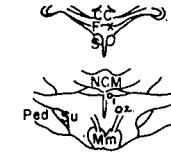**Septum 2 - 1600 μA/pulse**
1.
2.
3.
4.
5.

FIGURE 5. Comparison of shivering response to both septal and posterior hypothalamic stimulation. Stimulation of posterior hypothalamic locus 2 evoked well-defined shivering 22.3 hours after alpha chloralose administration (60 mg/kg I. P.). Ten minutes later, stimulation of septal locus 1 evoked, after a 20-second latency, a mild burst of shivering with a stimulus of double intensity. Forty-four seconds later (the break in the chart paper indicates a time interval of 30 seconds) there was a sustained burst of mild shivering. Since this activity was neither preceded nor followed by any such activity it is considered to have been due to the stimulus. Five minutes later stimulation of septal locus 2 evoked slightly more vigorous shivering using the same stimulus intensity. One hour later stimulation of posterior hypothalamic locus 1 evoked more intense and less latent shivering with a stimulus intensity half that necessary during septal stimulation. In the former three cases the rectal temperature was 37.8° C. In the latter case it was 1° C higher. The environmental temperature was constant at 28° C.

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suppression of shivering, when applied to an "active" locus, without a long post-stimulation period of suppressed shivering. Figure 6 illustrates this point.

Figure 7 summarizes the results for eight cats in which the septum was systematically explored for loci whose activation suppressed shivering. The results indicate that stimulation of ventromedial (loci 7, 8 and 16) and ventrolateral (loci 4 and 12) midseptal and posterior septal regions consistently evoked a suppression of shivering. Stimulation of extreme dorsal regions (loci 1, 5, 9 and 13) tended not to suppress shivering but some variability of response existed. Stimulation of intermediate regions (loci 2, 3 and 6) suppressed shivering in some cats and not in others. Stimulation of locus 11 never suppressed shivering although stimulation of locus 10 sometimes and locus 12 always suppressed it (Figure 8). In every experiment responses were reproducible. The responses evoked after bilateral fornical destruction were similar to those in which the fornices were intact (Figure 9). Similarly, the responses evoked in cat ST. 31 were relatively similar for both sides of the brain, even though the right side septum contained degenerated pre- and post-commissural fibers. The suppressive responses obtained from cats under alpha chloralose anesthesia were similar to those from preparations anesthetized with pentobarbital sodium. However, with alpha chloralose it was difficult to maintain a steady level of active shivering for the duration of the experiment. For this reason anesthesia with alpha chloralose was not used in experiments involving mapping for shivering suppression.

In these experiments the frequency of stimulation ranged from 25-100 p/sec and the pulse duration from 1-3 msec. In four experiments the minimum stimulus intensities necessary to evoke both strong and mild suppression of shivering at a variety of frequencies and pulse durations were noted. Less intense stimuli were necessary to suppress shivering at pulse durations of 3 and 5 msecs than at 0.5, 1 and 7 msecs. This appeared true for both septal and anterior hypothalamic suppression of shivering, although detailed observations were not made during septal stimulation. The intensity of stimulation necessary to suppress shivering was greater during septal than during anterior hypothalamic stimulation. The anterior hypothalamic loci stimulated were within the region found by others (Andersson et al, 1956; Hemingway et al, 1954; Magoun et al, 1938) to be most effective for inhibiting shivering. The septal loci were within the ventromedial region of the midseptum. Figure 10 is a schematic representation of the effects of alterations in stimulus frequency on the intensity of stimulation necessary to suppress shivering. Less intense stimuli were necessary to suppress shivering at stimuli frequencies of 25, 50 and 100 p/sec than at 10 and 200 p/sec. In two of the three experiments, stimuli of 100 p/sec were less effective than 25 and 50 p/sec stimulation. In cat ST. 33[a] both septal and anterior hypothalamic loci were stimulated, and again a greater stimulus intensity was necessary during septal stimulation.
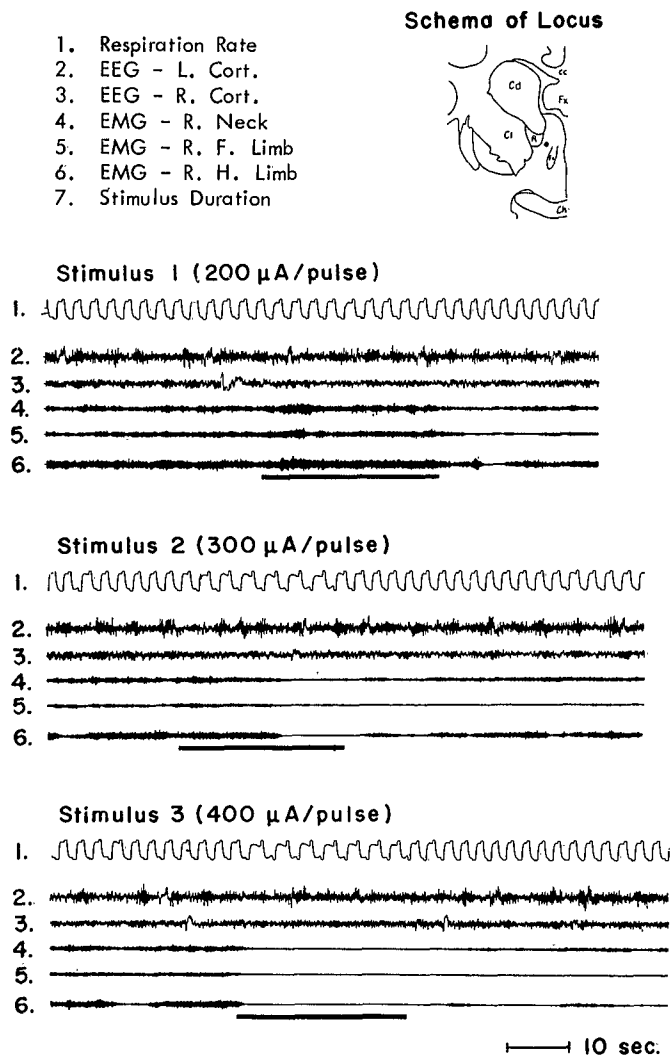
14

1. Respiration Rate
2. EEG - L. Cort.
3. EEG - R. Cort.
4. EMG - R. Neck
5. EMG - R. F. Limb
6. EMG - R. H. Limb
7. Stimulus Duration

Schema of Locus

Stimulus I (200 µA/pulse)

1.
2.
3.
4.
5.
6.

Stimulus 2 (300 µA/pulse)

1.
2.
3.
4.
5.
6.

Stimulus 3 (400 µA/pulse)

1.
2.
3.
4.
5.
6.

⊢——⊣ 10 sec.

FIGURE 6. Graded suppression of shivering during stimulation of a single anterior hypothalamic locus. In this experiment continuous shivering was evident in the waning stages of pentobarbital sodium anesthesia (35 mg/kg I. P.). Stimulation of a dorsal supraoptic locus evoked a short and mild suppression of shivering five seconds after the cessation of stimulation. The intensity of stimulation was 200 µ Amp/pulse. Five minutes later a stimulus intensity of 300 µ Amp/pulse applied to the same locus evoked a suppression of shivering in the latter half of the 30-second stimulation. Shivering resumed immediately after stimulation. Five minutes later stimulation of the same locus with a stimulus intensity of 400 µ Amp/pulse evoked immediate suppression of shivering, and it did not become active and continuous until 10 minutes after the cessation of stimulation. In all cases the stimuli had a frequency of 25 p/sec. and a pulse duration of 1 msec. On the basis of such observations it was decided to use a stimulus intensity that would evoke the second rather than the third suppressive response.

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CAT NO.		LOCUS															
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
ST. 12								+	++				++				+
ST. 18		O	++	++	++	O	++	++	++	O	+	O	+	O	+	+	++
ST. 19	L		O	O	O	O	O	+	+	O	+	O	+	O	+	+	++
	R		O	O	++		O	+	+	O	+	O	++	O	O	O	+
ST. 20			O	+	++		O	+	++								
ST. 22		O		O	+	O		++	++	O	O	O	++	+	+	+	O
ST. 27 *		+	+	++		+	+	+	+								
ST. 29 *		O	F	F			+	+	++	O	+	O	++	O	+	O	++
ST. 31 †	L		O		+		+		++		O		+		+		++
	R		+		++		O		++		+		++		O		++

O – No suppression
+ – Mild suppression
++ – Strong suppression
F – Facilitation
L – Left side stimulation
R – Right side stimulation
* – Bilateral fornical destruction
† – Right fornix destruction

Schema of Loci
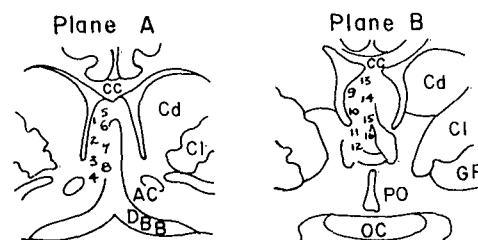Plane A   Plane B

FIGURE 7. Suppression of shivering during septal stimulation. The schemata of planes A and B and the loci numbers have already been described. A plane, intermediate to those shown, was systematically explored but the results were similar to Plane A. In cats ST. 19 and ST. 31 both sides of the septum were stimulated. Cat ST. 19 was under alpha chloralose anesthesia. In cat ST. 31 an attempt was made to destroy the right side fornix at a more caudal level one week prior to experimentation to permit degeneration of fornical projections. In cats ST. 27 and ST. 29 the fornix was cut bilaterally one week prior to experimentation. In this figure "mild" suppression means that shivering stopped for part of the stimulus duration. "Strong" suppression means that the activity was suppressed for the entire stimulus duration.
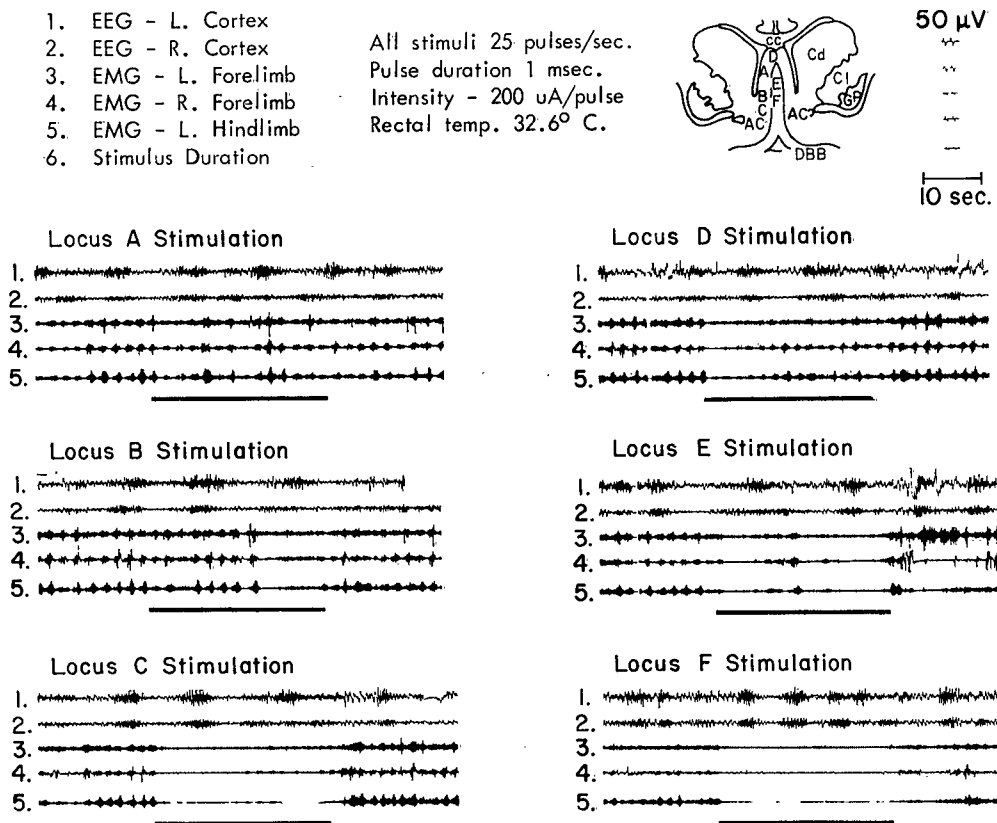
16

1. EEG - L. Cortex
2. EEG - R. Cortex
3. EMG - L. Forelimb
4. EMG - R. Forelimb
5. EMG - L. Hindlimb
6. Stimulus Duration

All stimuli 25 pulses/sec.
Pulse duration 1 msec.
Intensity - 200 uA/pulse
Rectal temp. 32.6° C.

50 μV

10 sec.

Locus A Stimulation

1.
2.
3.
4.
5.

Locus D Stimulation

1.
2.
3.
4.
5.

Locus B Stimulation

1.
2.
3.
4.
5.

Locus E Stimulation

1.
2.
3.
4.
5.

Locus C Stimulation

1.
2.
3.
4.
5.

Locus F Stimulation

1.
2.
3.
4.
5.

FIGURE 8. Suppression of shivering during septal stimulation of an intact brain. In this experiment spontaneous shivering resulted in the waning stages of pentobarbital sodium anesthesia (35 mg/kg). Each 5th minute a locus was stimulated in the order A, B, C, D, E and F. As shown, shivering was not suppressed during stimulation of locus A. It was mildly suppressed during stimulation of B, D, and E and strongly suppressed during stimulation of C and F.
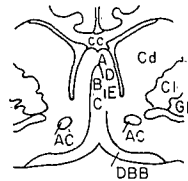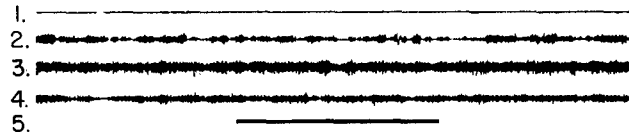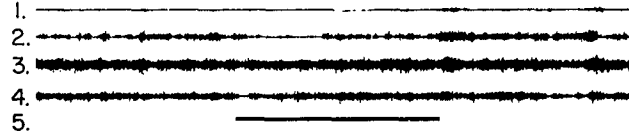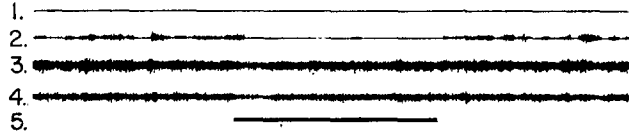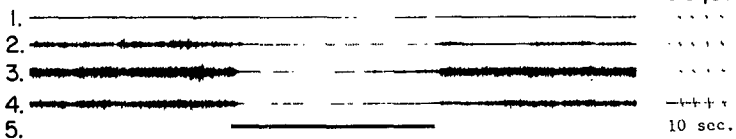
FIGURE 9. Suppression of shivering following bilateral fornical destruction. Photographs in the upper righthand corner illustrate partial left fornix destruction at a slightly more rostral level than the more complete right fornix destruction. Loci were stimulated each 5th minute in the order A, B, C, D and E with stimuli of frequency 25 p/sec., 1 msec. pulse duration and 800 μ Amp/pulse. Shivering was not suppressed by stimulation of loci D and E, mildly suppressed by stimulation of A and B and strongly suppressed by stimulation of C.
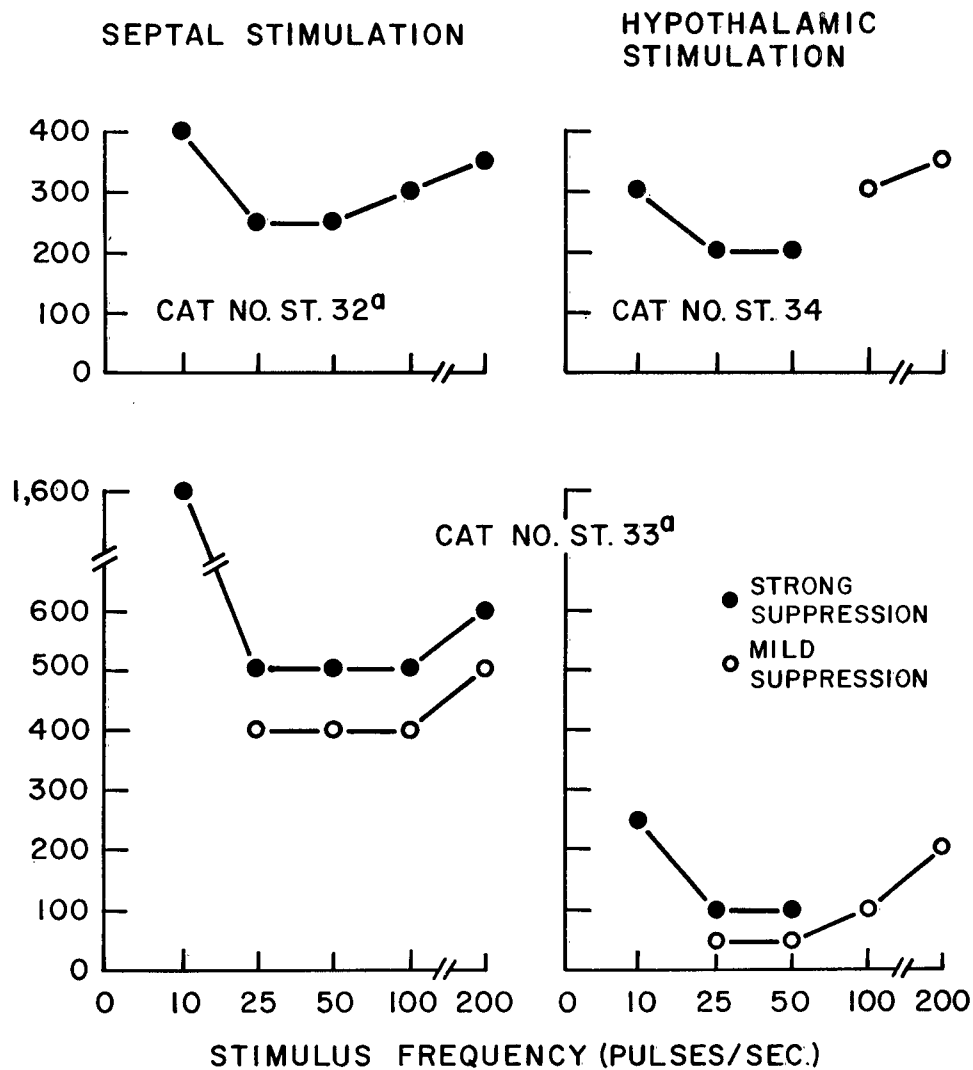
18

FIGURE 10. Effects of altering stimulus frequency on shivering suppression evoked during septal and anterior hypothalamic stimulation. The graph ordinate is stimulus intensity in μ Amp/pulse. The pulse duration was 3 msec. Septal loci were ventromedial and hypothalamic loci within the "heat loss center."

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During experiments on the inhibition of shivering, the dorsomedial region of the posterior hypothalamus was routinely stimulated to produce augmented shivering. It was observed that ventrolateral posterior hypothalamic stimulation suppressed shivering. Four experiments were conducted to compare the ratio of stimulus intensities necessary to suppress shivering during anterior and posterior hypothalamic stimulation and during septal and anterior hypothalamic stimulation. The ratio of stimulus intensities for the same suppression of shivering at the two sites septum/anterior hypothalamus was 5. 0 in cat S T. 33[a] and 2. 0 in cat S T. 34. (Figure 11). A similar intensity ratio for ventrolateral posterior hypothalamus/anterior hypothalamus was 1. 7 in cat S T. 36, 1. 0 in cat S T. 37 for right side stimulation and 1. 5 for left side stimulation. In all experiments in which shivering was suppressed by ventrolateral posterior hypothalamic stimulation, it could be evoked by dorsomedial posterior hypothalamic stimulation.

As with the production of shivering, bilateral suppression of shivering was evoked by ipsilateral stimulation. Variability existed as to the extent to which right and left fore- and hindlimb shivering was suppressed either strongly or mildly. No consistent pattern emerged during these experiments. Similarly, some variability existed as to the extent of forelimb vs hindlimb shivering suppression but no consistent pattern was evident.

In these experiments the inhibition of shivering was generally accompanied by a slowing of respiration and heart rate. Alterations in fronto-occipital EEG waves were not obvious during such stimulation but such parameters were not systematically studied in the course of these experiments.


SECTION 4. DISCUSSION

Effective Hypothalamic Region for Production of Shivering

The results on anesthetized animals suggest a localization of the production of shivering by electrical stimulation to neurons within the dorso-medial region of the posterior hypothalamus. More recently this has been confirmed by stimulation of unanesthetized animals (Stuart et al, 1962) and by lesion experiments (Stuart et al, 1961b). In this region no nucleus stands out in sharp relief from the dense neuropil of finely myelinated and unmyelinated fibers in which the cells are embedded. It includes part of the posterior hypothalamic nucleus, the dorsomedial edge of the field of Forel, the dorsal aspect of the supramammillary commissure and the posterior periventricular tract. Additionally it includes a narrow zone immediately ventral to the posterior reuniens nucleus of the thalamus. This

20
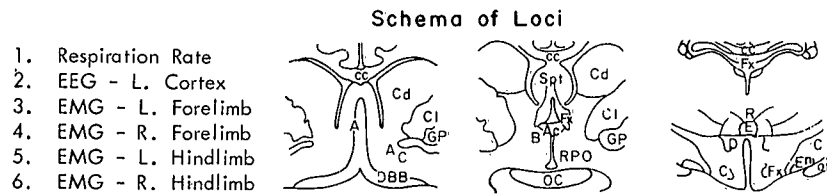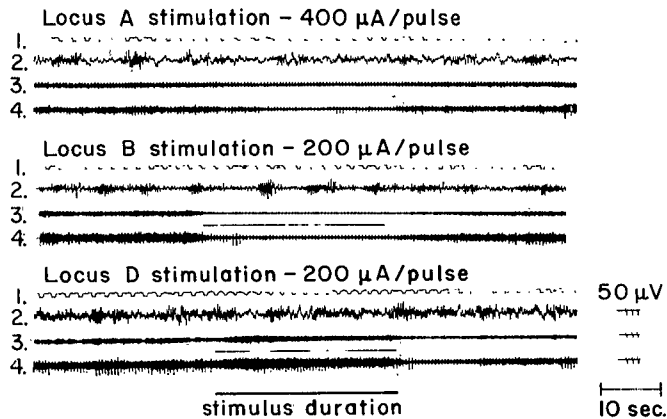
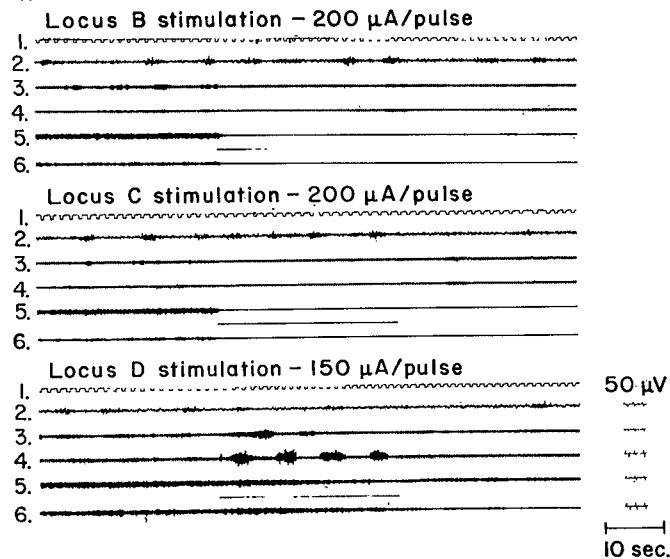FIGURE 11. Effects of septal, anterior and posterior hypothalamic stimulation on spontaneous shivering. In all cases loci were stimulated at 5-minute intervals and the frequency of stimulation was 25 p/sec. with a 3 msec. pulse duration. A represents a ventromedial mid-septal locus, B a "heat loss center" locus, C a ventrolateral posterior hypothalamic locus, and D a dorsomedial posterior hypothalamic locus.

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zone contains two-way connections between the midbrain and the basal ganglia and rhinencephalon (Adey, 1959; Adey and Lindsley, 1959; Bodian, 1946). Caudal outflows from the region are mainly to the dorsal longitudinal bundle of Schütz. It is unlikely that stimulation of the region evokes shivering by activation of neurons originating in more rostral structures because all such structures can be ablated without affecting the onset of cold-induced shivering in unanesthetized preparations.

During stimulation of this region heart respiration rate and EEG changes suggested a state of arousal. This region lies within what Hess (1957) has termed an ergotropic (work-producing) zone of the hypothalamus, in which activation of neurons produces (a) increased respiratory activity, (b) increased blood pressure, (c) increased heart rate, (d) pupillary dilation (e) increased motor excitability and sometimes flight. The only trophotropic (energy-restoring) responses he found in stimulating this region were urination and defecation. These were more evident in stimulation of the anterior hypothalamus, where ergotropic responses were less evident. Hess's results are based on stimulation of over 3,500 diencephalic loci in 350 cats. Shivering was observed during stimulation of but one such locus (medial posterior hypothalamus) in but one cat. He used a stimulator that could deliver variable intensity direct current mechanically interrupted 4-15 times/sec. Our results suggest that stimuli of 25-50 p/sec are the more effective for the production of shivering and that the lower stimulation frequencies used by Hess prevented his observation of this response.

Ranson and Magoun (1939) have reviewed the effects of hypothalamic stimulation with stimulus parameters similar to those used in this study. Their report includes 60 papers from other laboratories and their own results for the stimulation of over 7,000 loci in 50 anesthetized cats. That they did observe shivering was probably due to their use of animals under deep anesthesia (usually pentobarbital sodium) or to the lack of data on unanesthetized animals with electrodes implanted in the dorsomedial posterior hypothalamus. Their review cites responses similar to those reported by Hess. More recently, Starzl, Taylor and Magoun (1951) reported bilateral cortical activation during ipsilateral dorsomedial posterior hypothalamic stimulation (see their Figure 4D). Von Euler and Soderberg (1957) reported similar cortical activation during hypothalamic cooling. Their work indirectly suggests an increase in gamma efferent discharge during this cooling, and Granit and Kaada (1952) have evoked a similar increase during electrical stimulation of the exposed dorsal posterior hypothalamus. The increase in gamma efferent discharge would increase the bias on muscle spindles and may help explain how the rhythm of shivering is controlled proprioceptively (Perkins, 1945; Stuart et al, 1962).

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Bilateral Response to Ipsilateral Stimulation

Shivering seemed to appear bilaterally during ipsilateral brain stimulation. Differences sometimes observed in the vigor and duration of shivering during ipsilateral stimulation were not consistent. It is well known that shivering is more intense in limbs bearing less of the animals weight. In the course of an experiment there may have been minor shifts in the weight distributed to the four limbs. This could alter the proprioceptive inflow to create the observed differences in the shivering response in the four limbs.

Optimal Stimulus Frequency to Evoke Shivering

Our results agree with the findings of Birzis and Hemingway (1957a) in suggesting stimuli of 25-50 p/sec as optimal for producing shivering. This is in contrast to the shivering limb tremor frequency of 9-11 c/sec. Perkins (1945), Kawamura et al (1954) and Lippold, Redfearn and Vuco (1959) have shown that deafferentation alters the frequency and amplitude but does not abolish shivering. This suggests that the neural regulation of the rhythm of shivering is peripheral and proprioceptive dependent whereas its instigation is central. For shivering to be instigated certain neurons must be activated and such neurons probably have an optimal stimulus frequency that can vary over a limited frequency spectrum.

Production vs. Suppression of Shivering

It is necessary to discuss the seeming contradiction between the present results and those of Birzis and Hemingway (1956; 1957a; 1957b). They described a pathway mediating impulse related to the production of shivering, whose rostral extent embraced the ventrolateral posterior hypothalamus. Shivering was abolished for one to four hours after bilateral destruction of this region. Single unit discharges from within this region were recorded. They commenced or increased in frequency when shivering began. Shivering was also produced by electrical stimulation of loci along the midbrain and pontile passage of this pathway. However, the only hypothalamic loci whose activation evoked shivering were of ventrolateral rather than dorsomedial location. Our present results implicate the dorsomedial region in the production of shivering and the ventrolateral region in its suppression. Figure 12 illustrates an experiment that suggests a conflict of interpretation rather than experimental results. This experiment repeated our results of (1) the production of shivering during dorsomedial posterior hypothalamic stimulation; (2) the suppression of shivering during ventrolateral posterior hypothalamic stimulation; (3) normal shivering in chronically maintained cats with ventrolateral posterior hypothalamic destruction.
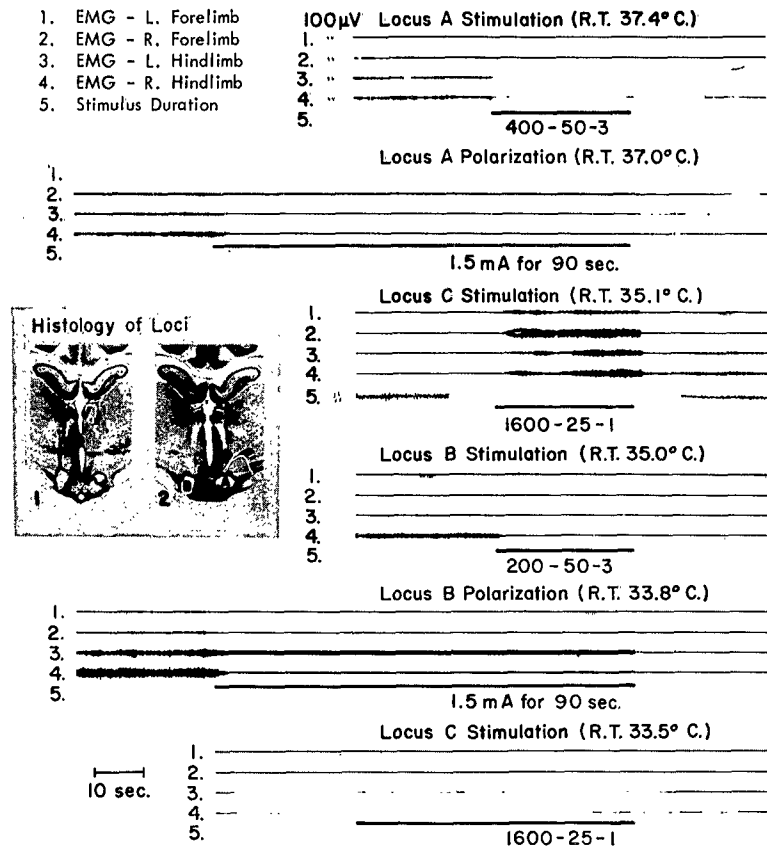
1. EMG - L. Forelimb
2. EMG - R. Forelimb
3. EMG - L. Hindlimb
4. EMG - R. Hindlimb
5. Stimulus Duration

100 μV Locus A Stimulation (R.T. 37.4° C.)

400-50-3

Locus A Polarization (R.T. 37.0° C.)

1.5 mA for 90 sec.

Locus C Stimulation (R.T. 35.1° C.)

Histology of Loci

1600-25-1

Locus B Stimulation (R.T. 35.0° C.)

200-50-3

Locus B Polarization (R.T. 33.8° C.)

1.5 mA for 90 sec.

Locus C Stimulation (R.T. 33.5° C.)

10 sec.

1600-25-1

FIGURE 12. Suppression of shivering during both stimulation and electrol-
ysis of ventrolateral posterior hypothalamic regions. Bipolar electrodes
were inserted into ventrolateral posterior hypothalamic loci (the center of
lesions noted with insets "A" and "B"). Another electrode was inserted into
the dorsomedial posterior hypothalamus (tip of electrode tract noted "C").
With the brain intact, 30-second stimulation of locus A at 50 3-msec.
pulses/sec. suppressed ongoing shivering in the cat anesthetized with pento-
barbital sodium (35 mg/kg I. P.). Shivering returned after 10 minutes and
was again suppressed when locus A was destroyed by electrolyzing current
of 1.5 mAmp. dc. The current passed between the electronegative bared
outer concentric tip of the bipolar electrode to an indifferent positive tongue
electrode for 90 seconds. The shivering was suppressed for 30 minutes but
was reproduced by stimulating locus C at 1600 μ Amp/pulse with 25 1-msec.
pulses/sec. Spontaneous shivering returned after this stimulation and was
suppressed by locus B stimulation. It was then reproduced by locus C stim-
ulation (not shown) and again suppressed by locus B electrolysis. Following
bilateral ventrolateral posterior hypothalamic destruction shivering did not
return while the animal was anesthetized, but 31 days after surgery it was
immediately apparent on exposure of the cat to cold, the ratio of oxygen con-
sumption rate shivering/resting being 3.2.

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It also confirms Birzis and Hemingway's demonstration of the suppression of shivering immediately after ventrolateral posterior hypothalamic destruction in the anesthetized cat. The failure of shivering to occur immediately after bilateral ventrolateral posterior hypothalamic destruction may have been due to cardiovascular depression.

This suggests the need for caution in interpreting the immediate results of tissue destruction in acutely anesthetized cats. The reason for functional differences between acute and chronically maintained lesion preparations is not clear. Perhaps the process of electrolysis stimulates the environs of the region being destroyed such that, if on a suppressive pathway, suppression continues after the cessation of polarization. A second alternative is that electrolytic lesions might produce some toxic substance peculiar to burned tissue. This has recently been proposed by Leonard and Bach (1960). They demonstrated that coma induced by destruction of large parts of the midbrain tegmentum involved extravasation of erythrocytes in the residual intact tegmentum. When a similar amount of tissue was removed by aspiration neither extravasation nor coma resulted.

Septal vs Hypothalamic Control of Shivering

The results listed in Table II suggest that shivering is more consistently produced during hypothalamic than during septal stimulation. When shivering was produced during septal stimulation it had greater latency of onset and/or required a greater stimulus intensity. This is in keeping with anatomical evidence (Nauta, 1958) that all known ventro-caudal septal projections relay in the hypothalamus. This suggests that to produce shivering during septal stimulation a greater temporal and/or spatial summation is necessary. The difficulty of consistently producing shivering during septal stimulation may be due to projections from the septum relaying in the anterior, as well as the posterior, hypothalamus.

Akert and Kesselring (1951) reported production by shivering by stimulation of 10 septal loci and one hypothalamic locus in eight cats. They thought the septum was primarily implicated in the production of shivering because Hess's results, from which their report derives, contained only one example of hypothalamic stimulation producing shivering. As mentioned above, this may have been due to the use of unfavorable stimulus parameters. Andersson (1957) reported the consistent and repeatable production of shivering during septal stimulation in three unanesthetized goats. He speculated that "it might be possible that an integrative action of all mechanisms concerned with heat conservation is exerted in this part of the forebrain." He did not compare the shivering response produced by septal and posterior hypothalamic stimulation. The fact that shivering occurs after transection separation of the anterior from the posterior hypothalamus (Bazett et al, 1933) suggests that structures more rostral than the posterior hypothalamus are not essential for the production of shivering.

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The evidence listed in Figures 4 and 7 seems to conflict with the results of Jacobson, Craig and Squires (1960). Our results show shivering to be produced by lateral septal stimulation and suppressed by medial septal stimulation. Jacobson, Craig and Squires suppressed it by electrolytic lesions of the medial septal region in anesthetized shivering cats. Figure 13 illustrates an experiment demonstrating that the interpretation, not the results, conflict.

Suppression of Ongoing Shivering

It was previously shown that a higher stimulus intensity was needed to evoke shivering during septal than during hypothalamic stimulation. The results on shivering suppression are similar. It is known from Kaada's report (1951) that fornical or hippocampal stimulation can suppress shivering. The experiments on cats ST. 27, 29 and 31, in which fornices had been cut and efferent projections degenerated, show that shivering suppression produced by medial septal stimulation was not dependent upon activating fornical fibers passing through the septum to the hypothalamus or midbrain. The relation of septal suppression and facilitation of shivering to the amygdala is obscure. McLean and Delgado (1953) suppressed shivering by stimulation of the basomedial complex of the amygdala. Koikegami, Hiroshi and Kimoto (1952) could not elevate body temperature by stimulating this complex but could do so by stimulating the lateral complex of the amygdala. This may mean that stimulation of separate amygdaloid structures can either facilitate or suppress shivering. This has never been shown. Such impulses could be carried by the direct diffuse amygdaloid projections to the hypothalamus (Fox, 1940) or by the stria terminalis, which Fox (1943) has shown to be efferent from the amygdala and which Ban and Omakai (1959) and Hall (1960) have shown to receive medial and not lateral amygdaloid projections. It is not known whether the amygdaloid activity related to the suppression of shivering exerts an influence upon the septum by way of the diagonal band of Broca. Earlier anatomists considered this band to form two-way connections between the amygdala and the medial septum. However, recent reviews of Ban and Omakai and of Hall suggest this tract is afferent to, not efferent from, the amygdala. In this study distinction has not been made between stimulation of neurons of septal origin and neocortical projections to the hypothalamus that traverse the septum. It is clear that telencephalic structures other than the septum are involved in the modulation of shivering. Further studies of this type might lay the groundwork for the neurological explanation of alterations in shivering by hypnotic suggestion (Gessler and Hansen, 1927) and Pavlovian conditioning of temperature regulation (Bykov, 1957).

The suppression of shivering by stimulation of the ventrolateral posterior hypothalamus confirms the results of Hemingway, Forgrave and Birzis (1954). (See their Table 1 and Figure 2.) This locus is within the projection

Septal-preoptic Lesion

R. Septal Stimulation-1600μA/pulse

1.

L.P. Hypothalamic Stimulation-800μA/pulse

2.

R. Septal Polarization-1mA for 90 sec.

3.

L.P. Hypothalamic Stimulation-1600μA/pulse
(Post Bilateral Septal Destruction)

Hypothalamic Stimulation

4.

|——————|
10 sec.

All stimuli 50 pulses/sec., 1 msec. pulse duration.
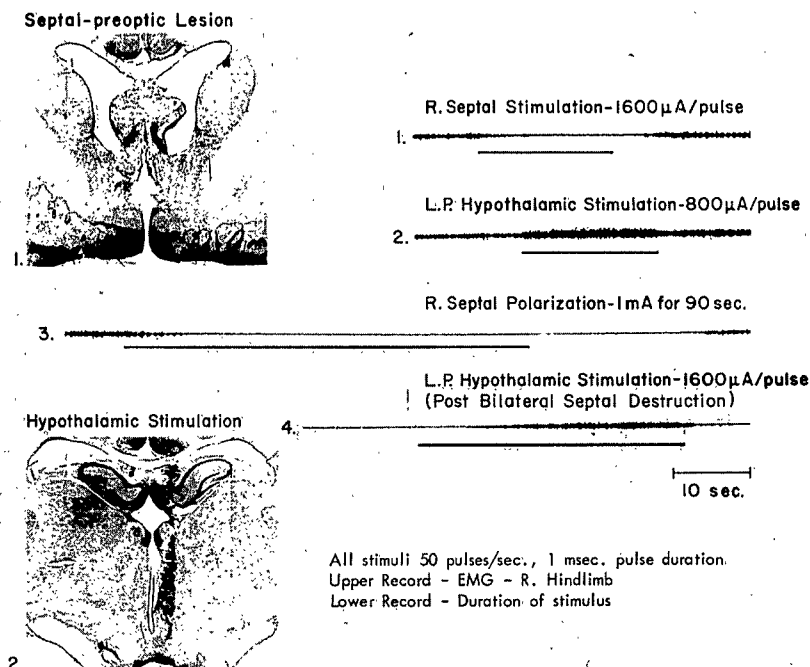Upper Record - EMG - R. Hindlimb
Lower Record - Duration of stimulus

FIGURE 13. Suppression of shivering during both stimulation and electrolysis of ventro-medial posterior septal region. Bipolar electrodes were inserted bilaterally into approximately the center of the forebrain lesion shown in the upper photograph. The tracts of the electrodes do not appear because the brain was sectioned at a different angle to the electrode paths. A bipolar electrode was also inserted into the posterior hypothalamus, as indicated by the black stain in the lower photograph. (Unfortunately, this electrode slipped medially while being removed; hence the stain shows a vertical and slanted angle to the electrode tract.) This cat was anesthetized with pentobarbital sodium (35 mg/kg I. P.) and when shivering began the following sequence of stimuli were applied: (1) 1600 μ Amp/pulse stimulation of the right medial septum to suppress shivering; (2) 800 μ Amp/pulse stimulation of the posterior hypothalamus to augment shivering; (3) right medial septal destruction by cathodal polarization of the electrode to suppress shivering for the 90-second duration of the stimulus, with the same destruction on the left side to produce a lesion the extent of which is shown in the upper photograph and which suppressed shivering completely; (4) reproduction of shivering by 1600 μ Amp/pulse stimulation of the posterior hypothalamus for the 60-second duration of the stimulus. After bilateral medial septal destruction the animal shivered only when the posterior hypothalamus was stimulated. However, four days later, when unanesthetized, the animal shivered vigorously on exposure to cold, the ratio of oxygen consumption rate shivering/resting being 3. 7.

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of forebrain bundle to and from the midbrain. Stimulation of this locus probably suppresses shivering, not via the anterior hypothalamus but rather by way of structures more caudal to the hypothalamus. The intensity of stimulus necessary to suppress shivering during stimulation of the locus was no greater than that needed during anterior hypothalamic stimulation.

In the present experiments there was evidence of a second system of suppressive neurons that perhaps originate in the anterior hypothalamus and terminate in the posterior hypothalamus. Stimulation of the most medial parts of the dorsal posterior hypothalamus required greater intensity to suppress shivering than did stimulation of the ventrolateral region at the same frontal level. Since this dorsal region is within that wherein activation produces shivering, there remains the possibility that the stimulus to it was also disrupting ongoing activity related to the production of shivering. This type of inhibition would be analogous to Wedensky inhibition of the spinal cord and has been observed by others (Lilly, 1957) upon stimulating central structures. Against this explanation is the observation that stimulation of loci 0. 25 to 0. 5 mm more lateral augmented rather than suppressed shivering. Moreover, shivering was suppressed from all loci within the dorsomedial region with 200 p/sec stimuli but was augmented with 25 p/sec except for stimulation of the most medial portion. This suggests that the anterior hypothalamus might suppress shivering by way of a dorsomedial as well as ventrolateral projections. In chilled cats and dogs, shivering can be suppressed by application of a warm stimulus to a very small surface of the body. Conceivably such a stimulus is sufficient to activate those neurons which suppress shivering after ventrolateral posterior hypothalamic passage. While such suppression is being mediated, the hypothalamic neurons responsible for the production of shivering are still being activated by the cold blood and/or sensory skin impulses but presumably attenuated by dorsomedial projections from the anterior hypothalamus.

Birzis and Hemingway (1957a) reported that shivering was best produced by stimuli of 25 p/sec and best suppressed by stimuli of 200 p/sec. Their conclusion conflicts with the results shown in Figures 3 and 12, which indicate that the optimal stimulus frequency is about 50 p/sec for both activation and suppression. In the present experiments shivering was suppressed during stimulation of the dorsomedial region of the posterior hypothalamus at 200 p/sec, but augmented at 50 p/sec. In the anterior and ventrolateral posterior hypothalamus, stimulation with both frequencies suppressed shivering but less intense stimuli were necessary at 50 than at 200 p/sec. This suggests that in studying the neurogenesis of suppressor mechanisms a distinction must be made between suppression caused by activation of a suppressor region and suppression cuased by disruption of the normal activity of an activator region.

SECTION 5. CONCLUSIONS

Shivering is produced by activation of cells within the dorso-medial region of the posterior hypothalamus (Figure 14). The activation of cells within this region is necessary to initiate and maintain shivering but not to regulate its rhythm.

The intensity of stimulation necessary to suppress shivering is the same in the ventro-lateral posterior hypothalamus and in the "heat loss center" of the anterior hypothalamus. This suggests that the outflow from the anteriorly situated "heat loss center," that is related to shivering suppression, is by way of the ventro-lateral posterior hypothalamus.

Shivering can be initiated, facilitated or suppressed by activation of septal neurons (Figure 15). Such activity is secondary to hypothalamic modulation of shivering. Stimulation of the septum evokes many other functions primarily integrated by the hypothalamus. When the septum is partially or totally destroyed, cold-induced shivering is of normal intensity (Stuart et al, 1961b). This supports the general body of literature concerning the physiology of the septum and other limbic structures. Such structures can be shown to affect functions controlled by the hypothalamus, but if these structures are ablated the hypothalamus is still capable of integrating the function. This fact has evidently been overlooked by previous investigators who have ventured to suggest that the septum is the primary "heat conservation center" of the homeotherm.
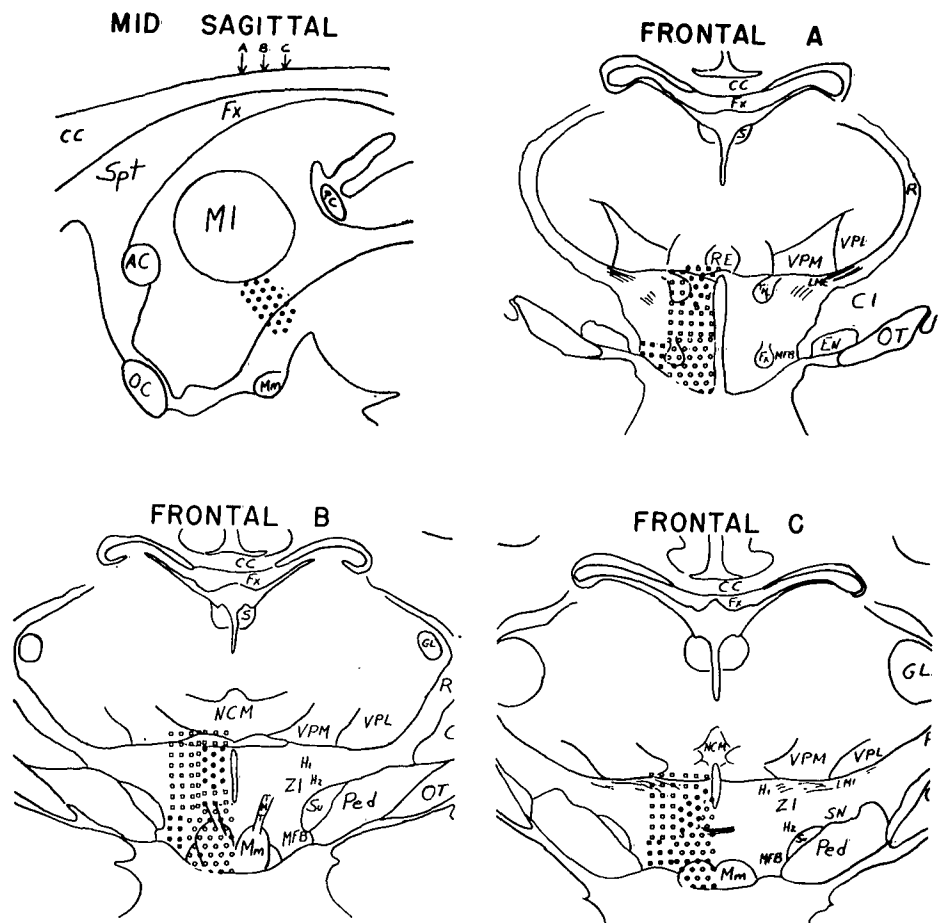
FIGURE 14. Summary of responses to posterior hypothalamic stimulation. Filled-in circles: Shivering. Hollow circles: No response. Hollow squares: Increase in muscle tone. Filled-in squares: Suppression of shivering.
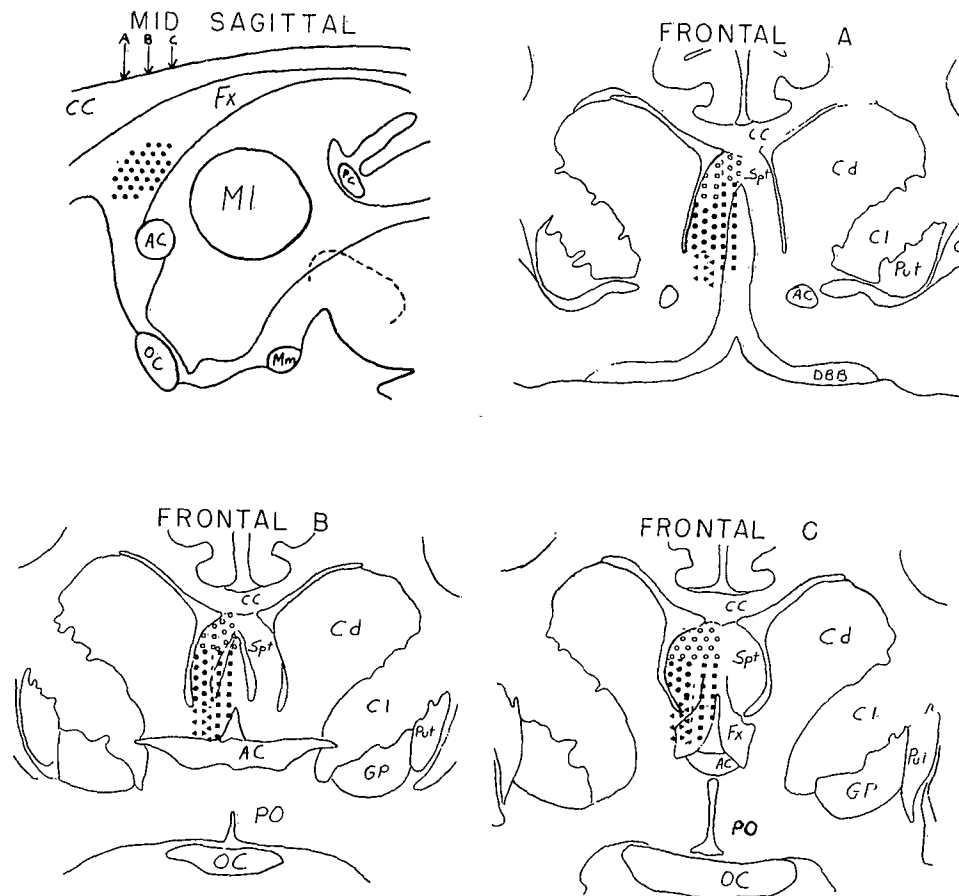
30

FIGURE 15. Summary of responses to septal stimulation.
Filled-in circles: Shivering. Hollow circles: No response.
Filled-in squares: Suppression of shivering. Hollow triangles:
Shivering or its suppression.

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Arctic Aeromedical Laboratory, United States Air Force (AFSC), APO 731, Seattle, Wash. Rpt. AAL-TDR-62-16. ACTIVATION AND SUPPRESSION OF SHIVERING DURING SEPTAL AND HYPOTHALAMIC STIMULATION. September 1962. 36 p. incl. illus, tables, 57 ref.

Unclassified Report

In acute experiments on 38 lightly anesthetized cats, the septal region of the forebrain and the hypothalamus were explored for loci whose activation by electrical stimulation produced, suppressed or failed to affect shivering. Shivering was consistently and repeatedly produced by stimulation of the dorso-medial region of the posterior hypothalamus, and sometimes by stimulation of the ventrolateral region of the septum. A greater intensity of stimulus was needed to produce more latent and less intense shivering during septal than during hypothalamic stimulation. Similarly, more intense stimulation was

necessary to suppress shivering during ventromedial septal stimulation than during anterior, or ventrolateral posterior hypothalamic stimulation. The most effective stimulation frequency for both activation and suppression of shivering was 50 pulses/sec, i.e. fivefold the evoked or suppressed limb tremor frequency. On the basis of these results it was concluded that septal influences on shivering are secondary to a primary hypothalamic modulation of this tremor. Such modulation appears to be more concerned with initiation and maintenance than with the rhythm of shivering.

1. Shivering
2. Hypothalamus
3. Cats
4. Brain
5. Stimulation
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